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Lupus Vulgaris Treated with Calciferol

By G. B. Dowling, M.D., and E. W. Prosser Thomas, M.D.

Dr. Prosser Thomas: We are presenting these cases of lupus vulgaris because of their good response to the oral administration of calciferol as virtually the only form of treatment. We have been treating lupus with calciferol since 1943. Including the six cases shown here to-day, we now have records of thirty-eight lupus patients who are being treated exclusively with calciferol or being followed up after stopping it.

It was Dr. Dowling who began giving calciferol in lupus, and the first patient to be treated with it is among those demonstrated to-day. [Case I.]

Case I.—Sidney B., aged 30. This man was attending St. Thomas's Hospital with confluent lupus of the face. He had been receiving intensive treatment elsewhere for the previous five years, including daily carbon arc baths and applications of Finsen light two or three times a week. He had also had injections of Alepol and of N.A.B. His lupus, however, which had begun near the right ear when he was 20, had steadily extended and for the past nine months his whole face had been in a congested and œdematous state and showed no signs of subsiding. In August 1943, Dr. Dowling began giving him calciferol, 50,000 i.u. three times a day in tablet form. After taking these for a few days he said that he developed nausea and felt generally ill and had to go to bed. His face got worse, the congestion increasing and exudation began. He discontinued the calciferol and stayed in bed for a fortnight. By then the congestion had subsided and he noticed that his lupus had improved, so much so that he began taking the calciferol again of his own accord. In a month or so, however, he had a second flare-up in the face, associated with general malaise, though less severe. He again discontinued the calciferol temporarily. He has tolerated the drug well ever since, except for occasional slight "stomach disorder". His lupus continued to regress and after a few months the dose of calciferol was reduced to 50,000 i.u. twice daily. By July 1945 there were only two rather doubtful lupus nodules to be found; his skin otherwise was comparatively clear and showed only soft and very superficial scarring. The calciferol was then reduced to one dose of 50,000 i.u. a day, on which he continued until October 30, 1945, when he was taken off it altogether. His serum calcium on that date was 14·8 mg. per 100 c.c. Apart from the two questionable nodules in the right cheek, which have remained unchanged for some months, his lupus appears to have cleared completely.

Case II.—Miss Jane P., aged 71, another of the cases presented to-day, was of a very similar congested type. She had had lupus for about five years. Her whole face, like that of Dr. Dowling's patient, had become distressingly angry and swollen and there was superficial ulceration of the cheeks, nose, and upper lip. The nasal mucosa was also involved, and the septum perforated. I first saw her in November 1944 and put her on calciferol, 150,000 i.u. daily, together with zinc cream and soluble sulphacetamide 5% to use as nasal plugs so as to try and clear up the secondary infection in the nose, which was practically blocked up with crusts. Her skin showed rapid response and by March 1945 was virtually clear, as it is to-day. She discontinued calciferol at that time and has shown no signs of relapse. The drug has never upset her.

Case III.—Miss Emma C., aged 72. In contrast to the above two acute forms of lupus, this patient had a large plaque of lupus tumidus in the glabellar area, which had been present without appreciable change for about thirty years. She also had superficially ulcer-

ative lupus of the lobe of the left ear and adjacent skin, still mildly active and showing nodules. She had not had treatment of any kind for many years. I first saw her in July 1944 and gave her calciferol, 150,000 i.u. daily. By September 1944 the lesions were showing obvious response and the dose was reduced to 100,000 i.u. daily. The lupus continued to regress slowly and she was kept on this dose until August 1945, when it was further reduced to 50,000 i.u. daily, which she is still taking. The glabellar lesion is now quite flat and shows mainly residual staining. There is still slight activity in the lower portion of the lesion. The ear lesions have completely healed and no nodules can be found. Her serum calcium level on October 31, 1945, was 10·5 mg. per 100 c.c. She has never been upset by the drug.

CASE IV.—Arthur M., aged 41. Extensive sheet of lupus on upper and inner aspect of right thigh, slowly progressive. Whole area thickened and raised, dusky red and rather scaly, resembling widespread lichenification. Section showed typical tuberculous structure. No previous treatment of any kind.

January 2, 1945: Given calciferol, 150,000 i.u. daily. At the end of the month the lesion showed response, being flatter and paler.

February 12, 1945: Dose reduced to 100,000 i.u. daily. Continued on this until August 13, 1945, since when he has been taking only one dose daily of 50,000 i.u. Serum calcium level on June 25, 1945, was 10·6 mg. per 100 c.c. By October 29, 1945, the whole lesion was flat, with residual pigmentation and islands of pink, clear, slightly atrophic skin. Serum calcium on that date: 10·1 mg. per 100 c.c. No intolerance to drug.

CASE V.—Mrs. Elizabeth G., aged 65. First seen December 12, 1943, with superficially ulcerative lupus of bulbous portion of nose and nasal vestibules of eight years' duration. She was treated until April 1944 with applications of liquid acid nitrate of mercury and radiostoleum by mouth with some response. Was then given calciferol, 100,000 i.u. daily until December 1944, when she ceased attending of her own accord because her nose had improved so much that it did not worry her any more. No intolerance to drug.

July 1945: No clinical lupus.

October 1945: Well. Serum calcium 11·2 mg. per 100 c.c.

CASE VI.—George Y., aged 45. Lupus involving whole of left ear and adjacent skin, twenty years' duration. More recent patch left malar area. All lesions active, with ulceration and crusting along helix.

First seen May 4, 1945. Confirmatory biopsy (left side neck). Calciferol given, 100,000 i.u. daily and continued ever since.

July 9, 1945: Good response. No further crusting and ear thinner and softer. Biopsy (apex of pinna, to exclude epithelioma because of thickening): Tuberculous histology.

Serum calcium, August 14, 1945 (after 100,000 i.u. calciferol daily approx. three months): 10·8 mg. per 100 c.c.

October 29, 1945: All lesions practically healed except for apex of pinna which is still crusting and slightly infected. No intolerance to drug at any time.

Of the other thirty-two cases, demonstrable improvement of varying degree has occurred in twenty-one cases, viz. of the total number of thirty-eight cases in which calciferol has been tried, there has been a favourable response in twenty-seven (approximately 71%). As regards the remaining eleven cases, in some calciferol has produced little appreciable change; in others, its effect has been difficult to assess, either because the lupus has more or less burned itself out or has become masked by previous scar-producing treatment of one kind or another, or by chronic radiodermatitis. Amongst the first-mentioned was the case of a child, a girl aged 10, who had a single small plaque of lupus in the right cheek of about one year's duration. We gave her calciferol, 50,000 i.u. daily for two months, at the end of which the lesion appeared a little flatter and paler. However, in view of the poor state of her general health we decided she needed full institutional treatment and arranged for her admission to the Treloar Home at

Alton. This was the only case in which we have had an opportunity of trying calciferol in lupus in childhood and in an early stage.

Comment

Calciferol (vitamin D_2) is a potentially toxic drug. It is a purely artificial substance, prepared by exposing the vegetable sterol, *ergosterol,* to ultraviolet light. It is said to be almost always contaminated with other possibly toxic by-products of irradiation, and to be more toxic than the naturally occurring vitamin D_3, which is found in animal products such as egg-yolk, butter, and fish liver oils, and is derived from irradiated animal sterols (Bicknell and Prescott, 1942).

Though apparently never tried hitherto in lupus, calciferol has been used in a variety of other diseases, often in very high dosage, and toxic symptoms have been observed not infrequently and reported in the literature. General well-being and a good appetite are said to be often the first symptom of poisoning. Anorexia may follow, together with nausea, vomiting, diarrhœa, and polyuria. Mental depression and headache may be early symptoms. Excessive doses mobilize phosphorus and calcium, thus broadly having an opposite effect to normal doses and producing metastatic calcification of soft tissues; of these, the renal tubules and arterioles and the media of the large blood-vessels are most affected. If the toxic doses are stopped the calcareous deposits are said almost to disappear. The serum calcium and phosphorus tend to be grossly raised, but not always—so that the serum calcium level is not a reliable guide. Serum calcium estimations in 12 of our cases after varying dosage and periods on the drug showed levels of between 10·1 and 10·8 mg. per 100 c.c. in 6 cases; in 3 cases the levels were approximately 11 mg., and in 3 cases there was hypercalcæmia, viz. 12·6, 13·8, and 14·8 mg. per 100 c.c. respectively.

From a review of the clinical results of many workers who have used calciferol in diseases such as chronic arthritis, Bicknell and Prescott (1942) found that most patients tolerated calciferol in doses of from 200,000 to 400,000 i.u. daily. They quote Steck and collaborators as stating, from extensive observations on over seven hundred patients, that few show toxic symptoms unless the dose exceeds 10,000 i.u. daily per pound of body-weight. Bicknell and Prescott, however, think these doses are far too high. From the clinical point of view they conclude (1) that, if large doses must be given it is useless to rely entirely upon blood calcium estimations as a safeguard, the clinical symptoms of poisoning being a better guide; (2) that the giving of highly concentrated vitamin D and calcium preparations together is unwise; (3) that fish liver oils should be the source of high doses of vitamin D; (4) that in patients with nephritis or cardiovascular disease large doses are unwise.

Regarding our patients, there have been symptoms of intolerance in eight of the thirty-eight. However, apart from Dr. Dowling's first case, who said he was severely upset on two occasions, the symptoms have been mild, consisting chiefly of nausea, loss of appetite, depression, or feeling out of sorts. We attributed the nausea mostly to simple irritation of the drug on the gastric mucosa, as it generally was felt soon after ingestion and then passed off. The symptoms have occurred usually in patients taking 150,000 i.u. daily, but the toxic threshold is said to vary considerably.

References

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Dr. J. E. M. Wigley: I think we are all agreed that the results of this treatment, demonstrated by these six cases, is most striking; one might almost say epoch-making. The lady (Case II) I saw at Charing Cross Hospital about two years ago when she had a definitely florid type of lupus vulgaris affecting her face. As she lives at Luton, and travelling conditions were very difficult at that time, and she was 70 years of age, I told her that I did not think any more could be done than was being done then. To-day I see her, to all intents and purposes, cured!

I think not the least important aspect of this treatment is an economic one. Treatment of lupus by other methods, e.g. Finsen light, general U.V.L., &c., has always had the great disadvantage of being very costly, both in apparatus and staff required, and in the patient's time, including loss of earning capacity. I do not wish to say that we can now dispense with these methods of treatment, but if the response to calciferol shows the continued, generally excellent results demonstrated to-day, a great advance will have been made in the method of dealing with this very serious social menace.

Dr. P. J. Feeny: I saw Case I several times when he was having Finsen light, and have not seen him again until now, when he is greatly improved.

Dr. R. M. B. MacKenna: There is some evidence that dermatologists in France are working along the same or similar lines and therefore I would urge Dr. Dowling and Dr. Prosser Thomas to publish an account of their work at an early date. I should like warmly to congratulate the exhibitors of these cases on the excellent results which they have achieved.

The President: We all congratulate Dr. Dowling and Dr. Prosser Thomas very sincerely. These cases are absolutely dramatic. I have not seen anything so promising for very many years.

Dr. G. B. Dowling: I have little to add except to thank Dr. Prosser Thomas for all the trouble he has taken in collecting and keeping records of these cases. Those that have been shown to-day have had no treatment whilst under our care except calciferol by mouth, but they are selected cases. As regards the other cases which we have treated with calciferol I think it is fair to say that all of them appear to have improved, but by no means all to the same extent.

Lupus Vulgaris Verrucosus of the Buttocks.—H. Corsi, F.R.C.S.

G. P., male aged 49.

Examination.—On the medial part of the buttocks are symmetrical areas, of a dark red, vegetative state of the skin, each area being rather larger than the size of a hand and fingers. The lesions are abruptly marginated, the margins appearing much more active than most of the central area, where some places show spontaneous recovery.

There is a clear area between the medial margin of each lesion and the anal skin. Rectal examination was negative.

There is a patch of lichenification on the left shin, which has been present for twenty years. This has given no trouble except some itching, which, following some X-ray treatment, has now ceased completely.

The Wassermann reaction is negative.

History—statement by patient.—He was never conscious of anything abnormal until the early part of 1945. From 1941 to June 1944 he used to go to business in his car, but after that he took to riding a bicycle. Some six months later, he noticed blood on his underclothing, and found some blood blisters on the inner surface of his buttocks. Excepting for some soreness, the condition gave him no trouble, and was only seen by his general practitioner, Dr. Hector of Letchworth, in June 1945, when the patient was examined on account of lumbago.

He was in the Army in 1939-41, and went to France. He had a fall from a wagon early in 1940, suffering severe bruising of the buttocks. This took several weeks to clear, but the patient says that after some months there was nothing left to see of this bruising. He has always been in good health except for "bronchitis", which troubles him most winters. His mother and brother died of tuberculosis. An X-ray photograph of his chest shows a large cavity in the left upper zone.

Examination of the small quantity of sputum which he was able to produce shows the presence of tubercle bacilli. The E.S.R. rate is 12 mm.

Diagnosis.—Chronic phthisis, probably of many years' standing.

Treatment.—There was improvement following the use of penicillin cream, which was tried in the belief that the condition might be a staphylococcal vegetative condition. There was improvement, also, in two smaller areas treated with X-rays.

Section.—The appearances are typical of lupus vulgaris.

Now that I have seen Dr. Dowling's and Dr. Prosser Thomas's cases I shall certainly put him on calciferol, and I hope I may have an opportunity of bringing him up here again, when we may note the therapeutic result.

Dr. J. E. M. Wigley: Does anyone know of the use of calciferol in tuberculosis in other parts of the body?

Dr. Prosser Thomas: I have not seen any references to its use in concentrated form in tuberculosis elsewhere.